



Southern European Regional Workshop
Defining the needs and means for more
Partnership between Patients, Patient Organisations
and Other Stakeholders in Clinical Trials
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Why is Partnering in Clinical Trials Important?

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Why is Partnering in Clinical Trials Important?

History of Drug Development 1/4

- Over thousands of years, herbals were the basis of treatments. Their effects were observed and described by physicians, monks and interested lay people and the knowledge passed on from generation to generation.
- Only at the end of the 19th century biologically-active organic molecules began to be isolated in relatively pure form for medicinal use (e.g. salicylic acid, morphine, codeine, quinine).



Why is Partnering in Clinical Trials Important?

History of Drug Development 2/4

- The first (semi-)synthetic drugs were antibiotics in the 1930s and 1940s followed by vitamins, vaccines, oral contraceptives, and tranquilizers (Valium®).
- Only as of the 1950s, drugs started to be developed for molecular targets.
- Drug approval processes were introduced based on proof of safety.



Why is Partnering in Clinical Trials Important?

History of Drug Development 3/4

- As a result of the Thalidomide tragedy, the FDA amended the US drug approval legislation in 1962 by requesting stronger safety demonstration but also proof of efficacy. National European legislation followed some years later.
- However, there was no methodology available to reliably prove efficacy. “Clinical Research” emerged as a scientific discipline to generate reliable information on new drugs.



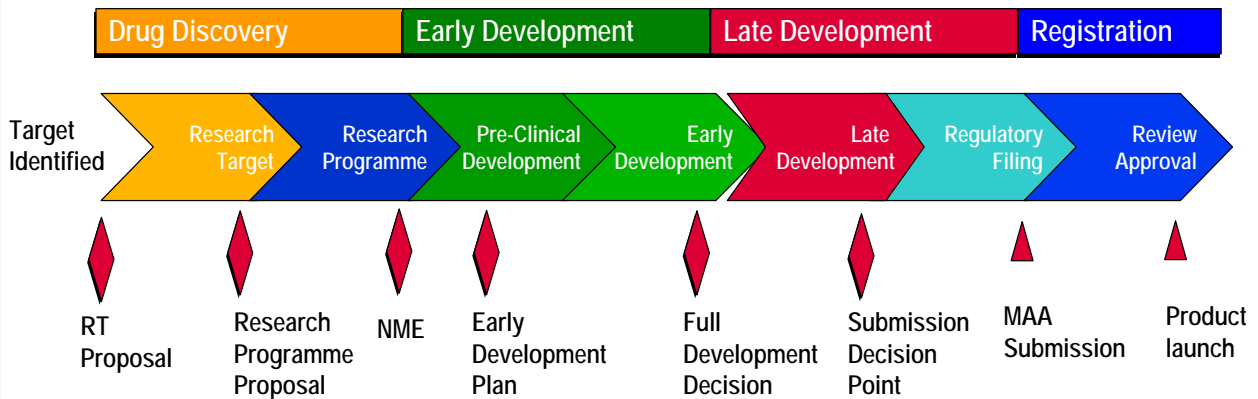
Why is Partnering in Clinical Trials Important?

History of Drug Development 4/4

- “Clinical Research” became a more and more sophisticated, very important part of the overall drug development process.
- Based on information from the pre-clinical/toxicological disciplines, the conditions were defined for when it was possible to do the first testing in men, mostly in healthy volunteers.
- Clinical development was divided in different phases.

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Drug Development Process





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Drug Development Overview

	Pre-Clinical Testing		Phase I	Phase II	Phase III		CA Approval	Total
Years	3-4	File 1st Study Approval	1	2 - 5	2 - 6	File Marketing Authorisation	1-2	10+
Success Rate	10,000 molecules evaluated		5 drugs enter clinical trials				1 approved	





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Phases of Clinical Drug Development

- Phase I:** First administration of a new drug in humans, usually in healthy volunteers.
- Phase II:** First evaluation of efficacy and safety in patients, dose finding.
- Phase III:** Large trials to confirm efficacy and safety under normal clinical conditions.
- Phase IV:** Evaluation of benefit/risk, cost/effectiveness, efficacy, safety and interactions in clinical practice after marketing authorisation.





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Essential Questions in Drug Development 1/2

- Drug development has the problem that it is not only necessary to find a molecule that is able to achieve the expected cure of the disease but this molecule needs to be applied in such a way that it enters the blood stream and arrives at the location where it should act.
- It is necessary to find the dose(s) in which the new drug acts without making (major) side effects.



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Essential Questions in Drug Development 1/2

- Many other questions need to be investigated like:
 - How does the drug work in elderly people or in children of different ages?
 - Does the drug show any interaction with other medications given to the same patient?
 - How good is the drug in comparison to standard treatment?
 - Does the drug have any negative long-term effects? Loose efficacy? Create resistance? Cause side effects?





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Study Design 1/2

- As “gold standard” in this new science, the concept of the controlled, randomised, double-blind clinical trial was developed by physicians, pharmacists and biologists, supported by statisticians and special experts like psychologists.
- It is necessary to objectively prove efficacy of a drug because history is full of treatments NOW known to be of no value or even harmful (e.g. Blood-letting).
- A new treatment should be compared against an established standard: CONTROL.



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Study Design 1/2

- “Randomisation” means: neither the physician nor the patient can choose which treatment the patient will receive; assignment to a treatment is done by hazard in form of a computer-generated treatment assignment list.
- “Double-blind” means: neither the physician nor the patient know which treatment the patient receives: test drug or standard treatment. This helps to avoid bias in judging the efficacy and tolerability of the treatments.



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Regulatory Requirements 1/2

- Once all required information on the drug has been generated and the effect of the drug has been demonstrated convincingly in at least two very large trials, the pharmaceutical company compiles all available data in a strictly structured way and submits this dossier either to a national competent authority or to the European Medicines Agency for review and approval.
- The Regulatory Authority performs a very thorough review of all data submitted, often performs an inspection of the pharma company and/or investigational sites.





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Regulatory Requirements 2/2

- If the outcome of the review is positive, the pharma company receives a marketing authorisation for a particular indication.
- If the company wants the drug to be administered in other indications as well, they need to perform clinical trials to prove efficacy and submit the data as basis for additional marketing authorisation in that new indication.
- There are special data requirements for drugs for rare diseases and faster approval processes for drugs with special medical need (e.g. Flu vaccines).





Why is Partnering in Clinical Trials Important?

Responsibility for Drug Development

- Nowadays, the overall responsibility for the performance of a clinical trial lies with the “sponsor.” This can be a pharma company or an academic institution.
- While drug discovery continued to happen at the universities, clinical development moved more and more to pharmaceutical companies with multi-functional dedicated resources, financial means and international reach to generate the data for marketing authorisation.



Why is Partnering in Clinical Trials Important?

Changes in Drug Development

- The development of “blockbusters” was the aim, the same drug for as many patients as possible. Today “personalised treatments” become more and more important.
- More and more legislation and regulatory framework was implemented to ensure the quality of methodology and data, to set the standards for marketing authorisation and to protect the participants in clinical trials.
- Thus, more and more expertise, resources and focus on management efficiency was required from the clinical researchers.





Why is Partnering in Clinical Trials Important?

Patients in Drug Development

- “Unfortunately” this new science “Clinical Research” needs human beings to be able to generate the required information and thus was faced from the beginning with an ever increasing level of ethical dilemmas.
- As of the late 1970s and in the 1980s, patients started to organise themselves in patient organisations with the aim to help each other, share information and identify clinical trials as a tool for access to new treatments – but not to change their role in clinical research.





Why is Partnering in Clinical Trials Important?

Current Situation in Drug Development

- Despite all scientific and managerial efforts, productivity in new drug development decreased and development costs exploded in the 1990s.
- New concepts are required to enhance drug discovery and clinical development.
- “New concepts” often means “new partners,” e.g. Biotech companies, CROs – and patient organisations.
- Patient organisations, especially in HIV and cancer indications, started to develop their organisations to partnership level.





Why is Partnering in Clinical Trials Important?

Who Would Benefit from Partnership With POs?

- Pharma companies could develop their drugs faster and at lower costs through improved patient recruitment and retention:
 - faster, more reliable access to patients,
 - better understandable patient information sheets,
 - protocols better adapted to clinical practice and patient needs,
 - better compliance with protocol requirements,
 - more reliable safety information,
 - improved image of clinical trials.





Why is Partnering in Clinical Trials Important?

Who Would Benefit from Partnership With POs?

- Pharma companies could strengthen their drug selection and development strategies:
 - identification of relevant indications;
 - identification of relevant drug features;
 - identification of most suitable patient populations for CTs;
 - identification of the most suitable countries for CTs;
 - more practice-relevant risk/benefit judgment;
 - more reliable safety information.





Why is Partnering in Clinical Trials Important?

Who Would Benefit from Partnership With POs?

- Pharma companies could improve their image:
 - through patients' better understanding of methodological issues,
 - through patients' better understanding of risks and benefits of drugs,
 - through provision of understandable, relevant information on disease and treatment options,
 - through regular meeting opportunities to enable asking questions and to give development updates, information on access to planned and ongoing trials.





Why is Partnering in Clinical Trials Important?

Who Would Benefit from Partnership With POs?

- Patient organisations could better serve their members:
 - more understandable information on the disease and treatment options;
 - opportunities to meet experts and ask questions;
 - more competent consulting by PO staff trained in CT methodology;
 - more professional organisation/dedicated staff to handle the PO tasks and increase awareness of existence due to stable financial conditions.





Why is Partnering in Clinical Trials Important?

Who Would Benefit from Partnership With POs?

- Patient organisations could better serve their members:
 - more information on clinical trial access opportunities;
 - selection of the most suitable trial for each patient;
 - reduction of risks in participating in a trial by patients' better understanding of the relevance of compliance.



Why is Partnering in Clinical Trials Important?

Who Would Benefit from Partnership With POs?

- Patient organisations could better serve their members:
 - “lobbying” for development of treatments in rare diseases;
 - enhanced availability of new treatments;
 - well trained PO staff representing their members’ interests and needs in ethics committees, DSMBs, regulatory authorities, etc.





Why is Partnering in Clinical Trials Important?

Who Would Benefit from Partnership With POs?

- Investigators could increase patient enrolment and retention:
 - faster, more reliable access to suitable patients;
 - better understandable patient information sheets;
 - shorter, more focused information process;
 - protocols better adapted to patient needs.

- Investigators could improve the quality of their data:
 - more reliable safety information;
 - better compliance with protocol requirements.





Why is Partnering in Clinical Trials Important?

Conclusions 1/2

- Partnership will make all 3 partners more successful in fulfilling their respective tasks.
- Selection of indications will be more relevant.
- Drug development will be faster and cheaper.
- Reliability of the data will increase.



Why is Partnering in Clinical Trials Important?

Conclusions 2/2

- Confidence in drug development will increase.
- Access to new treatments will be more transparent and fair.
- Patients' interests will be represented more strongly in the whole clinical development process.
- The new and so far mostly unknown challenges in the methodology of development of personalised medicines will require the concerted efforts of all 3 partners, willing to develop these treatment options together as quickly and successfully as possible.

